

Curriculum Vitae

Andrew Seth Greenberg

Current Address: 110 Rachel Road
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Work: Endocrine Division, New England Medical Center,
Jean Mayer USDA Human Nutrition Research Center on Aging
at Tufts University
Boston, MA 02111
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**Date & Place
of Birth:** April 1955
New Hyde Park, New York

Education: 1977, B.A., Amherst College, Amherst, MA
1981, M.D., New York University School of Medicine, New York, NY

Post-Graduate Training/Employment:

1981-84, Intern, Junior Resident, Senior Resident in Internal Medicine,
Hospital of the University of Pennsylvania, Philadelphia, PA

1984-87, Medical Staff Fellow, Diabetes Branch, National
Institute of Arthritis, Diabetes, and Digestive and Kidney Disease,
National Institutes of Health, Bethesda, MD

1987-91, Medical and Senior Staff Fellow, Section on Membrane
Regulation, Laboratory of Cellular and Developmental Biology, NIDDK,
National Institutes of Health, Bethesda, MD

1991-93, Expert, Section on Membrane Regulation, Laboratory of Cellular
and Developmental Biology, NIDDK, National Institutes of Health,
Bethesda, MD

1993-Present, Scientist II, Director, Program in Obesity and Metabolism,
Energy Metabolism Laboratory, USDA/HNRCA at Tufts University,
Director of Research, Obesity Consultation Center, New England
Medical Center, Assistant Professor, Endocrinology and Molecular
Medicine Tufts Medical School, Boston, MA

1995-Present, Assistant Professor, School of Nutrition
Science and Policy, Boston, MA.

Licensure and Certification:

1983, Medical License, Pennsylvania-MD-028859
1993, Medical License, Massachusetts-80352
1985, Diplomate, American Board of Internal Medicine,
Certification Number 100521
1987, Diplomate, Endocrinology & Metabolism Certificate Number
100521

Honors/Awards: 1976, March of Dimes Summer Student Fellowship
1977, Graduated cum laude with Honors in Biology,
1977-78, John Woodruff Simpson Fellow in Medicine,
Amherst College
1991, Henry Christian Award for Excellence in Research,
1999, Leon Kassel, MD Lectureship, "Obesity in 1999, Etiology, Therapy
and New Frontiers"
2001, Ray and Roy Kroc Lecture in Advanced Diabetes Research and
Visiting Professor at Stanford University School of Medicine,
"Molecular Regulation of Adipocyte Lipolysis: Implications for
Diabetes"

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Teaching:

1993-Present: Teach both in the Tufts School of Nutrition and Public Policy and School of
Medicine

Patents

1. Cloning of the perilipin proteins. Inventors: Constantine Londos, Andrew S. Greenberg,
Alan R. Kimmel, and John J. Egan
2. Methods for treatment of insulin resistance and related disorders. Andrew S. Greenberg-
patent application submitted.

Society Memberships

American Institute of Nutrition
North American Association for the Study of Obesity
American Diabetes Association
Endocrine Society

Journal Review

Diabetes
Journal of Clinical Endocrinology and Metabolism
Obesity Research
Journal of Lipid Research
Metabolism

Bibliography

1. Greenberg, A.S. Taylor, S.I., and Londos, C. Presence of a functional inhibitory GTP-binding regulatory component, G_i , linked to adenylate cyclase in adipocytes of ob/ob mice. *J Biol Chem* 1987;262:4565-4568.
2. Egan, J.J., Greenberg, A.S., Chang, M.K., and Londos, C. Control of endogenous phosphorylation of the major cAMP-dependent protein kinase substrate in adipocytes by insulin and β -adrenergic stimulation. *J Biol Chem* 1990;265:18769-18775.
3. Greenberg, A.S., Egan J.J., Wek, S.A., Garty, N.B., Blanchette-Mackie, E.J., and Londos, C. Perilipin, a major, hormonally-regulated, adipocyte-specific phosphoprotein associated with the periphery of lipid storage droplets. *Proc Natl Acad Sci, U.S.A.* 1991;88:11500-11504.
4. Nishimura, H., Saltis, J., Habberfield, A.D., Garty, N.B., Greenberg, A.S., Londos, C., and Simpson, I.A. Phosphorylation state of the glut4 isoform of the glucose transporter and subfractions of the rat adipose cell: Effects of insulin and isoproterenol. *Proc Natl Acad Sci, U.S.* 1991;88:11500-11504.
5. Egan, J.J., Greenberg, A.S., Chang, M.K., Wek, S.A., Moos, M.A., and Londos, C. Mechanism of hormone-stimulated lipolysis in adipocytes: Translocation of hormone-sensitive lipase to the lipid storage droplet. *Proc Natl Acad Sci, U.S.A.* 1992;89:8537-8541.
6. Greenberg, A.S., Nordan, R.P., McIntosh, J., Calvo, J.C., Scow, R.O., and Jablons, D. Interleukin-6 reduces lipoprotein lipase activity in adipose tissue of mice *in vivo* and in 3T3-L1 adipocytes: A possible role for IL-6 in cancer cachexia. *Cancer Research* 1992;52, 4113-4116.
7. Greenberg, A.S., Egan, J.J., Wek, S.A., Moos, M., Londos, C., and A. Kimmel. Isolation of cDNAs for perilipins A and B: sequence and expression of lipid droplet-associated proteins of adipocytes. *Proc Natl Acad Sci, U.S. A.* 1993;90: 12035-12039.
8. Blanchette-Mackie, E.J., Dwyer, N.K., Barber, T., Coxey, RA, Takeda, T., Rondonine, CM, Theodorakis, J.L., Greenberg, A.S., and C. Londos. Perilipin is located on the surface layer of the intracellular lipid droplets in adipocytes. *J Lipid Res.* 1995;36:1211-1226.
9. Roberts, S.B., Fuss, P., Dallal, G.E., Atkinson, A., Evans, W.J., Joseph, L., Fiatarone, M., Greenberg, A.S., Young, V.R. Effects of Age on Energy Expenditure and Substrate Oxidation During Experimental Overfeeding in Healthy Men. *J Gerontology*, 1996; 51:B148-157
10. Roberts, S.B. and A.S. Greenberg. Age-associated changes in energy regulation and their relation to mitochondrial DNA mutations. *Aging Clin Exp Res* 1995; 7:469-470.
11. Roberts, S. B. and A. S. Greenberg. The New Obesity Genes. *Nutrition Reviews*, 1996, 54: 41-49
12. Roberts, S.R., Nicoloson, M., Staten, M., Sawaya, A.L. Heyman, M.B., Fuss, P., Greenberg, A.S Total energy expenditure, but not metabolic rate is correlated with circulating leptin in humans. Relationship between circulating leptin and energy expenditure in adult men and women aged 18 years to 81 years. *Obesity Research*, 1997; 5:459-463
13. Souza, S.C., Yamamoto, M.T, Franciosa, Lien, P., and A. S. Greenberg. BRL 49653 Blocks the Lipolytic Actions of Tumor Necrosis Factor-alpha : A Possible New Insulin Sensitizing Mechanism for the Thiazolidinediones. *Diabetes*, 1998; 47:691-695
14. Fried, S.K., Bunkin, D.A., and A. S. Greenberg. Omental and subcutaneous adipose tissue of

obese subjects release interleukin-6: depot difference and regulation by glucocorticoid.
Journal of Clin Endocrinol and Metabolism , 1998,;83:847-850

15. Rosenbaum, S.E., and A. S. Greenberg. The short and long-term effects of tumor necrosis factor-alpha and BRL 49653 on PPAR γ 2 and other Adipocyte Genes. *Molecular Endocrinology*, 1998,; 12:1150-1160
16. Souza, S.E., Moitoso de Vargas, L, Moss, L.G. and A.S. Greenberg. Overexpression of perilipin A and B blocks tumor necrosis factor-alpha induced lipolysis. 1998; *J Biol Chem* 272: 24665-24669
17. Melanson KJ, Greenberg AS, Ludwig D, Saltzman E, Roberts SB. Blood glucose and hormonal responses to small and large meals in healthy young and older women. *J Gerontology* 1998,53A:B299-305
18. Bartholon GP, Tucker KL, Vinken LAG, GreenbergAS, Roberts SB. The accuracy of three common diet methodologies in postmenopausal women classified as restrained or unrestrained eaters. *Am J Clin Nutr* 2000 (in press)
19. McCrory MA, Fuss PJ, Hayes NP, Vinken AG, Greenberg AS, Roberts SB. Eating out and overeating in America: association between restaurant food consumption and body fatness in healthy adult men and women aged 18-80. *Obesity Research* 1998,7:564-571
20. Moriguti JC, Das SK, Saltzman E, Corales A, McCrory MA, Greenberg AS, Roberts SB. Effects of a 6-week hypocaloric diet on changes in body composition, hunger and subsequent weight regain in healthy young and older adults. *J Gerontology* 2000 (in press)
21. Heymsfield SB, Greenberg AS, Fujioka K, Dixon RM, Kushner R, Hunt T, Lubina JA, Patane J, Self B, Hunt P, McCamish M. Recombinant leptin for weight loss in obese and lean adults. A randomized, controlled, dose-escalation trial. *JAMA* 1999, 282:1568-74
22. Bartholon GP, Tucker KL, Vinken LAG, GreenbergAS, Roberts SB. The accuracy of three common diet methodologies in postmenopausal women classified as restrained or unrestrained eaters. *Am J Clin Nutr* 2000. 71:739-45
23. Moriguti JC, Das SK, Saltzman E, Corales A, McCrory MA, Greenberg AS, Roberts SB. Effects of a 6-week hypocaloric diet on changes in body composition, hunger and subsequent weight regain in healthy young and older adults.. *Gerontol A Biol Sci Med Sci*. 2000 Dec;55(12):B580-7.
24. Rosenstock M, Greenberg AS, A Rudich. Distinct long-term regulation of glycerol and non-esterified fatty acid release by insulin and TNF-a in 3T3-L1 adipocytes. *Diabetologia*. 2001. 44:55-62.
25. Rudich A, Vanounou S, Riesenber K, Porat M, Tirosh A, Harman-Boehm I, Greenberg AS, Schlaeffer F, Bashan N. The human immunodeficiency virus protease inhibitor nelfinavir induces insulin resistance and increases basal lipolysis in 3T3-L1 adipocytes. *Diabetes*, 2001, 50:1425 1431.
26. Saltzman E, Das SK, Lichtenstein AH, Dallal GE, Corrales A, Schaefer EJ, Greenberg AS, Roberts SB. An Oat-Containing Hypocaloric Diet Reduces Systolic Blood Pressure and

Improves Lipid Profile beyond Effects of Weight Loss in Men and Women. J Nutr, 2001, 131: 1465-1470

- 27 Das SK, Moriguti JC, McCrory MA, Saltzman E, Mosun C, Greenberg AS, Roberts SB An underfeeding study in healthy men and women provides further evidence of impaired energy regulation of energy expenditure in old age. J Nutr, 2001, 131(6): 1833-8
- 28 Bathalon GP, Hays NP, Medyani SN, Dawson-Hughes B, Schaefer EJ, Lipman R, Nelson M, Greenberg AS, Roberts SB. Metabolic, psychological and health correlates of dietary restraint in healthy postmenopausal women. J Gerontol A Biol Sci Med Sci., 2001, 56(4):M206-11.
- 29 Saltzman E, Moriguti JC, Das SK, Corrales A, Fuss P, Greenberg AS, Roberts SB. Effects of a cereal rich in soluble fiber on body composition and dietary compliance during consumption of a hypocaloric diet. J Am Coll Nutr 2001, 20(1):50-7.
- 30 Atshaves BP, Stoery SM, McIntosh AI, Petrescu AD, Lyuksyutova OL, Greenberg AS, Schroeder F. Sterol carrier protein-2 expression modulates protein and lipid composition of lipid droplets. J Biol Chem, 2001, 276:5324-35
- 31 Faber BC, Cleutejens KB, Niessen RL, Aarts PL, Boon W, Greenberg AS, Kitslaar PJ, Tordoir JH, Daemen MJ. Identification of genes potentially involved in rupture of human atherosclerotic plaques. Circ Res 2001, 89:547-54.
- 32 Chen J-S, Greenberg AS, Tseng Y-Z, S-M Wang. Protein kinase C-regulated expression of adipose differentiation-related protein in sterol ester-laden RAW macrophages. J Cell Biochem 2001, 87: 99.
- 33 Greenberg AS, Shen WJ, Muliro K, Patel S, Souza SC, Roth RA, and FB Kraemer . Stimulation of lipolysis and hormone-sensitive lipase via the extracellular signal regulated kinase pathway. J Biol.Chem Oct: 2001 papers in press

Funding: ACTIVE

PI: Greenberg, AS	
1 RO1 DK50647-01A2	1/15/99-12/31/2002 65%
NIH/NIDDK	D: \$134,486 ID: \$103,366
The Role of the Perilipins in Adipocyte Lipolysis	\$1,097,998
 R00 PI: Greenberg, AS	 1/1/99-12/31/2001 10%
American Diabetes Association	D: \$85,000 ID: \$15,000
Structure/function analysis of the perilipins: lipid droplet-associated proteins that regulate TNF-induced lipolysis	\$300,000
 58-1950-9-001 (PI: I. Rosenberg, M.D.)	 10/01/98-9/30/99 5%
USDA Cris Contract	D: \$134,175 ID: \$21,468
Energy Regulation in Aging	

Invited Presentations:

Invited Talks/Meetings:

- 1) Clinical assessment of the obese patient. Invited talk at Obesity Update: assessment and Treatment of the Patient with Medically Significant Obesity. (Continuing Medical Education Course) Sacramento, California. October, 1991.
- 2) Perilipin: A lipid droplet-associated, hormonally-regulated phosphoprotein of adipocytes. Invited talk at symposium: application of new techniques study adipose tissue metabolism. Joint Annual Meeting of the North American Association for the Study of Obesity and The Society of the Study of Ingestive Behavior. October, 1991
- 3) Regulatory events at the surface of the lipid droplet in adipocytes-perilipin, a novel phosphoprotein. The Lipid Club of the George Washington University School of Medicine. March, 1991.
- 4) Trafficking at the surface of the lipid droplet in adipocytes: implications for the regulation of fat metabolism. Medical College of Pennsylvania. April, 1991.
- 5) Perilipin: a novel hormonally regulated, adipocyte-specific phosphoprotein located at the surface of the lipid storage droplet in adipocytes. Rockefeller-St. Luke's-Roosevelt Obesity Research Center, Rockefeller. 1991.
- 6) Greenberg, A.S. Perilipin-Endocrine Grand Rounds, Beth Israel Hospital, 1994.
- 7) Perilipins, a family of lipid droplet associated proteins-Tufts University Vascular Biology Seminar Series. 1994
- 8) Perilipins, a family of lipid-droplet associated proteins, a link between adipocytes and steroidogenic tissues: implications for regulation of intracellular lipid metabolism- Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University. 1995
- 9) Roberts, S. B. and Greenberg, A.S. Age-associated changes in energy regulation and their relation to mitochondrial DNA mutations, Meeting: Consequences of age change explored at the cellular and subcellular levels on organismic function. Volterra, Italy. 1995
- 10) Perilipins, a family of lipid-droplet associated proteins, a link between adipocytes and steroidogenic tissues: implications for regulation of intracellular lipid metabolism. Endocrine Grand Rounds, NEMC, May, 1995.
- 11) Molecular Regulation of Lipolysis, GRASP Center Grand Rounds. 9/11/ 1995
- 12) Role of Perilipins in Lipid Metabolism. Plenary Speaker, Woods Hole Meeting on Adipose Tissue, Boston Obesity Nutrition Research Center, 2/9/ 1995.

- 13) Molecular Regulation of Lipolysis: A Possible role for the perilipin family of proteins. Dept. of Biochemistry, Mt. Sinai School of Medicine, 12/11/1995.
- 14) Obesity, Medical Grand Rounds, NEMC, 3/1996
- 15) Chairperson, Session on Adipocytes and Diseases at the Keystone Symposia, The Adipose Cell: Molecular Aspects of Differentiation, Gene Expression, and Metabolic Regulation in the Normal Cell and Obese Models. 2/1997
- 16) Organizer and Chairperson, Diabetes and Metabolism Minisymposium, FASEB, ACN, 5/1997.
- 17) American Physiological Society, FASEB'98, Symposia: Pluripotent effects of tumor necrosis factor- α on insulin sensitive tissues., Talk: "Tumor necrosis factor regulation of adipocyte lipolysis" 4/1998
- 18) Advances in the Molecular Basis and Understanding of Obesity, Symposium: Obesity: Bridging the gap between research and clinical practice, JM-USDA HNRC at Tufts University, 6/1998
- 19) Regulation of Adipocyte Lipolysis, Novartis Pharmaceuticals Corporation, East Hanover, NJ, October, 1998, 10/98
- 20) Parke Davis Sponsored Symposium: Impact of TNF- α on Insulin Resistance: Role of the Thiazolidinediones, Ponte Verde, Florida, 11/1998
- 21) Hormonal Regulation of Adipocyte Lipolysis: Possible Role of the Lipid-Droplet Associated Proteins the Perilipins. Beth Israel Deaconess Endocrine Grand Rounds: 3/1999
- 22) Leon Kassel Lectureship, "Obesity in 1999: Etiology, Therapy, and New Frontiers Sinai Hospital, Baltimore, Maryland. 4/99.
- 23) Cytokines and Insulin Resistance, Meeting: The Insulin Resistance Syndrome: Molecular Mechanisms linking obesity, insulin resistance and cardiovascular disease, Cambridge, England. 5/1999
- 24) Clinical effects of leptin in humans, featured symposia. 81st Annual Meeting of the Endocrine Society, 6/1999
- 25) Regulation of adipocyte lipolysis. University of Vermont School of Medicine Endocrine Grand Rounds, Burlington Vermont, 3/2000.
- 26) Forum for Collaborative HIV Research on Adipocyte Biology, Washington, D.C. August/2000
- 27) Molecular regulation of adipocytes lipolysis and its potential implications for obesity related metabolic complications. Centre for Cardiovascular Genetics, University College of London, August, 2000
- 28) Adipose tissue as an endocrine organ: IL-6 in adipose tissue, North American

Association for the Study of Obesity Annual Meeting. October, 2000.

- 29) Identifying the links between insulin resistance and beta-cell function: the role of cytokines in peripheral tissues/organs. Insulin Resistance and Beta-Cell Function Think Tank. October, 2000 Newport, Rhode Island. Sponsored by SmithKline Beecham
- 30) Diabetes, Obesity, and Atherosclerosis: Inflammation, the Final Common Pathway? SmithKline Beecham, Upper Providence, PA. November, 2000
- 31) Molecular Regulation of Lipolysis. Endocrine Grand Rounds, Columbia University College of Physicians & Surgeons. January, 2001
- 32) Kroc Visiting Professorship at Stanford University School of Medicine, Molecular Regulation of Adipocyte Lipolysis and its Implications for Diabetes, April, 2001
- 33) Molecular regulation of adipocyte lipolysis and its implications for type II diabetes. New England Medical Center Endocrine Grand Rounds. May 8, 2001.
- 34) Perilipin regulates fat metabolism in cells and animals in symposium: Gene Regulation and Adipose/Lipid Metabolism-Lean Mice Models. North American Association for the Study of Obesity Annual Meeting. Quebec, Canada: October 9, 2001
- 35) Lipolysis: Players, Proteins and Pathophysiology. Adipose Tissue Study Group., Boston Obesity and Nutrition Research Center November 6, 2001.. Boston University
- 36) Regulation of Lipolysis: Implications for Insulin Resistance and Diabetes. Endocrinology Grand Rounds. Washington University School of Medicine. St. Louis, Missouri. November 8, 2001.
- 37) Perilipin, Potential Marker of Plaque Rupture: What is Perilipin? Why is it found in plaques? Vulnerable Plaque Detection and Treatment Program Lecture Series, Massachusetts General Hospital December 10, 2001

Abstracts:

Zhang HH, Halbleib M, and AS Greenberg. Regulation of basal and TNF-alpha stimulated lipolysis by activation of the extracellular signal related kinase pathway, counteregulation by rosiglitazone. 61st Scientific Sessions, Diabetes, 2001, A13:49-OR

Souza SC, Muliro K, Lien P, Halbleib M, Schaffer J, Liscum L, Obin M and AS Greenberg. Adenovirus expression of perilipin A modulates hormone-sensitive lipase-mediated lipolysis in NIH 3T3 ACS1/FATP1. 61st Scientific Sessions, Diabetes, 2001, A12:47-OR

Shen WJ, Muliro K, Halbleib M, Souza SC, Kraemer FB, and AS Greenberg. Extracellular related kinase increases adipocyte lipolysis by phosphorylating and activating hormone-sensitive lipase. 61st Scientific Sessions, Diabetes, 2001, A13: 51-OR.

Imachi H, Souto R, Kraemer FB, Syu L-J, Pilch P, and AS Greenberg. Hormone-sensitive lipase and lipotransin localize to a specific subcellular compartment to regulate adipocyte lipolysis. 61st Scientific Sessions, Diabetes, 2001, A13: 52 –OR.

Interleukin-6 increases lipolysis and leptin release in cultured human adipose tissue. Trujillo ME, Kalyoussef S, Brodin RE, Schneider SH, Greenberg AS, and S Fried. 61st Scientific Sessions, Diabetes, 2001, A13:48OR..

Wang Yanxin, Sullivan S, Trujillo ME, Brodin RE, Greenberg AS, and SK Fried. Dexamethasone regulates perilipin expression in human adipose tissue. 61st Scientific Sessions, Diabetes, 2001, A88:351-P

Faber BG, Cleutjens KB, Boon W, Kislal J, Tordoir JH, Greenberg AS, and MJ Daemen Ruptured plaque specific gene expression: a role for perilipin/ADRP and HSL mediated lipolysis? Circulation, 2001, 104:42A

Haffner SM, Greenberg A, Weston W, Fuell D, Chen H, and M Freed. Effects of rosiglitazone treatment on levels of C-reactive protein and MMP9 in patients with Type 2 Diabetes. Circulation, 2001, 104: 565 A.

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Exhibit I

Regulation of Basal and TNF- α -Stimulated Human Adipocyte Lipolysis by Activation of the Extracellular Signal-Related Kinase Pathway. Counterregulation by Rosiglitazone HUI H ZHANG, MELANIE HALBLEIB, ANDREW S GREENBERG, Boston, MA

The aim of the study was to examine the mechanisms whereby TNF- α regulates lipolysis in human adipocytes. Preadipocytes from human abdominal subcutaneous adipose tissue were differentiated into adipocytes and subsequently used for the study. TNF- α treatment (100 ng/mL) for 6-72h increased lipolysis by ~1.5-2.5 fold. Perilipin A (peri A) is a protein that localizes to the lipid droplet surface where it acts as a barrier to reduce the access of lipases to lipids. Phosphorylation of peri A leads to its disassociation from the lipid droplet surface and increased lipolysis. Coincident with the TNF- α mediated increase in lipolysis, western analysis demonstrated peri A migrated as a doublet consistent with hyperphosphorylation. TNF- α also activated extracellular signal-related kinase 1/2 (ERK), as demonstrated by phosphorylation of ERK1/2 on western analysis. The increase was maximal within 15-30 min, and remained detectable at 24h. To investigate whether the activation of ERK 1/2 is involved in TNF- α -stimulated lipolysis, adipocytes were treated with TNF- α in the presence/absence of PD98059 (100 μ M), a specific inhibitor of the ERK upstream activator mitogen activated protein kinase (MEKK) 1/2. PD98059 diminished TNF- α -induced-ERK and perilipin phosphorylation, increased perilipin expression by ~60%, and decreased lipolysis to below basal (non-TNF- α -treated) levels. PD98059 treatment alone also reduced basal lipolysis by 50-70%. Rosiglitazone (rsg) (5 μ M for 24h), a peroxisome-proliferator-activated receptor γ agonist, decreased basal (by ~40%) and TNF- α -induced lipolysis (to control levels) but had no significant effect on ERK 1/2 phosphorylation. Rosiglitazone thus counteracts the ERK mediated increase in basal and TNF- α -stimulated lipolysis. These findings suggest that the ERK pathway regulates both basal lipolysis and TNF- α stimulated lipolysis in human adipocytes. In addition, rsg reductions in basal and stimulated lipolysis are downstream from the ERK pathway.

Scientific Sessions, Diabetes (2001) A13:49-OR